

CATGAAGGTTCCCTCCTGTCCTGCTTCTCTTTCTTCTGTCCTCAGTGCGAGCTACTGAGCAACCGCAGGTGCTCACTG
 AGCATCCCAGCATGAGGCGAGCCCTGACCGGGGCCAAGCCCTCCTCGCACTTCTGGGGCAACTA~~CACT~~TTCTCTGAC
 TGGCAGAACTTCGTGGGCGAGGAGACGTTATGGGGCCGAGTCCCAGAAACCCACGGTGAAAGCACTGCTCATCGTGGC
 CTACTCATTACCATCGTCTTCTCGCTCTTCGGTAAATGTCCTGGTCTGTCATGTCATCTTCAAGAACCAGCGCATGC
 ACTCGGCCACCAGCCTCTTCAATTGTCAACCTGGCAGTGGCGGACATCATGATCACATTGCTCAACACGCCCTTCACT
 TTGGTCCGCTTTGTGAACAGCACATGGGTGTTTGGGAAGGGCATGTGTCATGTCAGTCGCTTTGCTCAGTACTGTTC
 TCTACATGTCTCAGCACTGACTCTGACAGCTATCGCAGTGGACCGCCACCAGGTTCATCATGCATCCACTGAAGCCTC
 GGATCTCCATCACCAAGGGTGTCATATATATTGCTGTCTCATCTGGGTTCATGGCTACCTTCTTCTCTCTGCCACATGCC
 ATCTGCCAGAACTGTTTACCTTCAAGTACAGTGAGGACATTGTGCGCTCCCTCTGCCTGCCGGACTTCCCGGAGCC
 AGCTGACCTCTTCTGGAAGTATCTGGACCTGGCCACCTTTCATCCTGCTCTACCTACTTCCACTCTTCATTATCTCAG
 TGGCCTATGCTCTGTGTGGCCAAGAAGCTGTGGCTCTGTAAACACCATTTGGCGACGTGACCACAGAGCAGTACCTCGCC
 CTGGGAGCGCAAGAAGAAGAACCCGTGAAGATGCTGGTGGCTGTGGTAGTCTCTTTGGCCCTGTGCTGGTTCCTCTCT
 CAACTGTATGTCTCTCTCTGTCTCAGCAAGGCCATCCACACCAACAATGCCCTCTACTTTGGCTTCCACTGCTTTG
 CCATGAGCAGTACTTGTATATAACCCCTTCATCTACTGCTGGCTCAATGAGAAGCTTTAGGGCTGAGCTTAAGGCATTG
 CTGAGCATGTGCCAAAGGCCACCCAAAGCCGCGAGGAAGACAGGCTACCTTCCCCAGTTCTTCTTCCAGGGTGGCATG
 GACAGAGAAGAGCCATGGTGGGAGGGCTCCACTACCTAATCACCACTTTGCCCTCTTCCCAGATCCAGTCTGGGAAGA
 CAGATCTGTCTCTGTGGAAACCCGTTGTGGCCATGAGTTAGGGAAAGCTGGAAGTTGGTGGGGGAGGGTTCTTTCTCT
 CTCACAATTGACCAGACACTAACAGAGTTGGAAAGTAACACAGAAAGCAGTGAGATGCTTTGGGTTCCTAGGAACCTGT
 CCAGCCCCATCTGATTTGCCAAACTTTCTAGAAGATGCCATGAGGTGGTCTGTGTAGATCTTTGAGCAAGAGCTCTGG
 AAACCACTCAGCTTCAACAGAGGCTGGTCCAGTCAACCACCTCCAATTGTGTAGCATCTGCCACCTTGGCCCTTCTCT
 ACTGCTGAGCAACCACAGGGGGACTTGAGCCATACTATTGGTGGGCCCTGCCCCACATGCTCAGAAAAGAACAGGCAC
 AAAGGCTTTCTGAAGTCATTGGAACAGGAATAATCACACAGCTTCAGTGACCTTGGCTCTATCCATGACCAGACAGG
 ACCCATTTTGGCTTCTTAAAAACAAAGAGAAATTAGTATTGCCACTTTGAAAAGTTTCAAGAAAAGTAAAGAAATGAGT
 TCAGCCCTCAATTTGTAAGAAAAAGGAAAAAGAAAAAGAAAAAGAAAAAGAAAAAGCCTGTTAATATGCTGTA
 AATTTATCTGTAGCTTTGGCTTCTGTGTGTGTACATTTGTACTTTTAAAAATCCTGAACTACACGTGTCCATGTAGAT
 TGTAAATAATTAGCAAGAACTGGAAATATATCAGAGTATTATTGAATTC (SEQ ID NO:1)

MKVPPVLLLFLSSVRATEQPQVVTEHPSMEAALTGPNASSHFWANYTFSDWQNFVGRRRYGAESQNPTVKALLIVA
 YSFITVSLFGNVLVCHVIFKNQRMHSATSLFIVNLAVADIMITLLNTPFTLVRFVNSTWVFGKGMCHVSRFAQYCS
 LHVSAITLTAIA/DRHQVIMHPLKPRISITKGVIYIAVIW/MATFFSLPHATCQKLFTFKYSEDIVRSLCLPDPFPEP
 ADLFWKYLDLATFILLYLLPLFIISVAYARVAKKLWLCNTIGDVTTEQYLALRRKKKTTVKMLVLVVVLFALCWFLPL
 NCYVLLSSKAIHTNNALYFAPHWFAMSSTCYNPFIYCWLNNENFRVELKALLSMCQRPPKPKQEDRLPSPVPSFRVAW
 TEKSHGRRAPLPNHLPSSQIQSGKTDLSSVEPVVAMS (SEQ ID NO:2)

FIGURE 1

Underlined = deleted in targeting construct

Bold = sequence flanking Neo insert in targeting construct

GGGGTGGCAGTCGGCACCATCAGGCTCCCTTGGCGTTTCGGAGTTTTCTCTGTGGTCCCG
 ACTCTCCGGAGGATCTCGGTTGTCTCCCAAGTCGGAACCTGGCACGGTCCAGGTTCACTC
 GGAGGTCCGGGCTTCCTCTGTGCCCCGTGCCCTCGCTCCCAGGCTCCCTCTGTGGTGTG
 GACTCCTCTAGCCCCGTGCGCTCAGCCCCCTCGCACCCAGCCTCCAGGCACAGAGCCCGGC
 AGGGAGCTCAGCCCTTGTGCCTAGAGCTGCAGTGGCTGGACATGAAGGTTCTCCTGTCC
 TGCTTTCTCTTCTCTGTCTCAGTGCGAGCTACTGAGCAACCGCAGGTCTCACTGAGC
ATCCAGCATGGAGGCAGCCCTGACCGGGCCCAACGCCTCCTCGCACTTCTGGGCAACT
ACACTTTCTCTGACTGGCAGAACTTCTGGGTCAGGAGACGTTATGGGGCCGAGTCCCAGA
ACCCCAACGGTGAAAGCACTGCTCATCGTGGGCTACTCATTACCATCGTCTTCTCGCTCT
TCGGTAATGTCTGGTCTGTCTATCTTCAAGAACCAGCGCATGCACTCGGGCCACCA
GCCTCTTCAATTGTCAACCTGGCAGTGGCGGACATCATGATCACATTGCTCAACACGCCCT
TCACTTTGGTCCGCTTGTGGAACAGCACATGGGTGTTTGGGAAGGGCATGTGTATGTCA
GTGCGCTTTGCTCAGTACTGTTCTCTACATGTCT**CAGCACTGACTCTGACAGCTATCGCAG**
TGGACCGCCACGGTCAATCATGCATCCACTGAAGCCTCGGATCTCCATCACCAGGGTG
 TCATATATATTGCTGTCTATCTGGGTCTATGGCTACCTTCTTCTCTCTGCCACATGCCATCT
 GCCAGAAACTGTCTTACCTTCAAGTACAGTGAAGGACATTGTGCGCTCCCTCTGCGTGGCGG
 ACTTCCCGGAGCCAGCTGACCTCTTCTGGAAGTATCTGGACCTGGCCACCTTCATCCTGC
 TCTACCTACTTCCACTCTTCAATATCTCAGTGGGCTATGCTCGTGTGGGCAAGAAGCTGT
 GGCCTCTGTAAACACCATTTGGCGAGCTGACCAACAGAGCAGTACCTCGCCCTGGGACGCAAGA
 AGAAGACCAACCGTGAAGATGCTGGTGGCTTGTGGTAGTCCCTCTTTGCCCTCTGCTGGTTCC
 CTCFCAACTGCTATGTCTCTCTTGTCCAGCAAGGCCATCCACACCAACAATGCCCTCT
 ACTTTGCCCTTCCACTGGTTTGGCATGAGCAGTACTTGTATAACCCCTTCATCTACTGCT
 GGCTCAATGAGAACTTTAGGGTTGAGCTTAAGGCATTGCTGAGCATGTGCCAAAGGCCAC
 CCAAGCCGCGAGGAAGACAGGCTACCCCTCCCCAGTTCCCTTCCCTCAGGGTGGCATGGACAG
 AGAAGAGCCATGGTGGGAGGGCTCCACTACCTAATCAACCACTTGCCTCTTCCCAGATCC
 AGTCTGGGGAAGACAGATCTGTCTATCTGTGGAACCCGTGTGGGCTATGAGTTAGGGAAAGC
 TGGAAAGTTGGTGGGGGAGGTTCTTTCTCTCACAATTGACCAGACACTAACAGAGTTGG
 AAAGTAACACAGAAAGCAGTGAGATGCTTGGGTTCCTAGGAACCTGTCCAGCCCCATCTGA
 TTTGCAAACTTTCTAGAAGATGCCATGAGGTGGTGTGTGTAGATCTTTGAGCAAGAGCTC
 TGGAAACCACTCAGCTTCAACAGAGGCTGGTCCAGTCAACCACCTCCAATTGTGTAGCA
 TCTGCCACCTTGCCTTCCCTACTGCTGAGCAACCAAGGGGACTTGAGCCATACTATTG
 GTGGGCTTGGCCACATGCTCAGAAAAGAACAGGCACAAAGGCTTTCTGAAGTCATTGGA
 ACAGGAATAATCACACAGCTTCAGTGACCTTGGCTCTATCCATGACCAGACAGGACCCAT
 TTTGGCTTCTTAAAAACAAAGAGAAATTAGTATTGCCACTTTGAAAAGTTCAGAAAAGTA
 AAGAAATGAGTTTACGCCCTCAATTTGTAAAAAAGGAAAAAAGAAAAAAGAAAAAAG
 AAAGAAAAAAGCCTGTAAATATGCTGTAAATTTATCTGTAGCTTTGCCTTCTGTGTGTGT
 ACATTTGTACTTTTAAAAATCCTGAACTACACGTGTCCATGTAGATTGTAATAATTAGCAA
 GAAACTGGAATATATCAGAGTATTATTGAATTC

FIGURE 2A

Gene Sequence Structure * 299 bp Sequence Deleted 753 bp

Size of partial
cDNA: 2253 bp



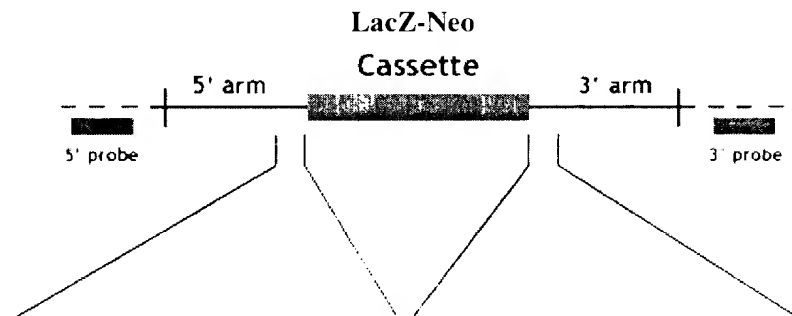
Targeting Vector*
(genomic sequence)

Construct Number: 463

Arm Length:

5': 2.5 kb

3': 0.6 kb



———— Targeting Vector
- - - - Endogenous Locus

* Not drawn to scale

5'>CTGGCACGGTCCAGGTTCACT
CGGAGGCCCGGGCTTCCTCTGTGC
CCCGTGCCCCCTCGCTCCCTGGCTC
CCTCTGTGGTGTGGACTCCTCTAG
CCCGGTGCGCTCAGCCCCCTCGCAC
CCAGCCTCCAGGCACAGAGCCCGG
CAGGGAGCTCAGCCCTTGTGCCTA
GAGCTGCAGTGGCTGGACATGAAG
GTTTCTCCTGT<3'
(SEQ ID NO:3)

5'>CAGCACTGACTCTGACAGCTA
TCGCAGTGGACCGCCACCAGGTGA
GAGCACCTGTCCCCAGCAGCATGC
TCCCATCTCCGTCTATGCCCTGGCT
GGCTGGTGGGAATACTGCCACCAC
GGTCTGTAGGGAATACTCTCAGGA
CAGTGACTCATTTCAGTCCCGCTGA
CAGCGTGTGTGCTTGCCCTCCTTGT
TGATCAATTTG<3'
(SEQ ID NO:4)

FIGURE 2B